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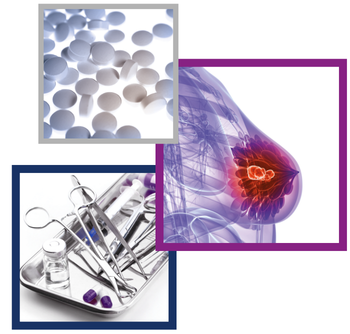
Breast Cancer Management



Outcomes of intraoperative versus preoperative ultrasound-guided wire localization of nonpalpable breast lesions

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Background: Nonpalpable breast lesions require localization, the gold standard for which is preoperative ultrasound-guided wire localization (PUGWL). Our unit also employs intraoperative ultrasound-guided wire localization (IUGWL). Here we evaluate PUGWL and IUGWL outcomes between 2014 and 2018. Primary outcomes were reoperation rates, complication rates and average specimen weights. Trainee feedback and cost analysis assessed IUGWL viability. **Methods:** Prospectively recorded data were collected. 511 patients were included (241 PUGWL and 270 IUGWL). **Results:** Reoperation rates: PUGWL 17.7% versus IUGWL 13.9% ($p = 0.28$). Complication rates: PUGWL 5.8% versus IUGWL 6.6% ($p = 0.72$). Average specimen weight: PUGWL 34.2 g versus IUGWL 24.3 g ($p < 0.0001$). Trainees needed 15 supervised cases to be IUGWL competent. Performing IUGWL saves £289 per localization. **Conclusion:** IUGWL outcomes are comparable to those of PUGWL. IUGWL is cost-effective, patient-friendly and easy to learn and replicate. IUGWL merits wider dissemination and further planned research.

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Keywords: breast cancer • breast conserving surgery • guidewire localization • intraoperative ultrasound • nonpalpable

Background

In 2017–18 the UK National Health Service Breast Cancer Screening Programme screened 2.14 million women, detecting over 18,000 breast cancers. 40.1% of these patients had small invasive cancers [1].

Our tertiary breast cancer unit treats around 500 cancers annually, 40% of which are screen detected. The vast majority of screen-detected lesions are nonpalpable lesions (NPL). Patients with partial or complete response to neoadjuvant therapy add to the number of NPLs treated.

NPLs require localization for breast-conserving surgery (BCS). Traditionally this is performed preoperatively by a Radiologist, using image guidance placing a guidewire into the lesion under local anesthetic. A mammogram then confirms guidewire placement.

Most lesions are ultrasound visible and this is the most commonly used imaging technique for guidewire localization [2–4]; it is faster than stereotactic guidance, and easily operated. Calcification and disease not sonographically visualized can be made localizable using a device often referred to as a marker clip [5,6]. The marker clip is placed in the center of the lesion at diagnostic biopsy. Further mammographic imaging ascertains if it is correctly positioned prior to localization. Patients undergoing neoadjuvant treatment have one or more marker clips deployed prior to commencing systemic treatment. The position of the marker clip, the size of the lesion and the relationship between the two are reassessed with ultrasound prior to surgery [7].

Patients having BCS for a NPL are kept busy on the day of surgery with trips to nuclear medicine, radiology and finally the operating theatre. They also potentially have two invasive procedures: ultrasound-guided localization

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with subsequent mammography and nuclear medicine injection for sentinel lymph node biopsy. This adds to the patient's anxiety, stress and physical discomfort.

A preoperative ultrasound-guided wire localization (PUGWL) is a costly technique requiring complex organizational arrangements around scarce resources in radiology departments. From a surgeon's perspective, guidewires carry the risk of displacement and migration [8–11] and may take a tortuous route through the breast, increasing the difficulty of BCS. Alternative isotope-based techniques for excision of NPLs, such as radio occult lesion localization or radioactive seeds, carry their own organizational difficulties and are increasingly difficult to implement due to regulations surrounding isotope use. Techniques such as magnetic seeds or radiofrequency transponder devices overcome some of these difficulties but require dedicated equipment and are usually priced to match the cost of a preoperative localization. All intraoperative localization techniques require additional training.

Ultrasound devices are used in multiple clinical settings and are increasingly readily available in many operating theatres. Demonstration of a known breast lesion is a basic function of breast ultrasound and can be employed intraoperatively to localize a NPL or marker clip [12–17]. While ultrasound alone can be used to locate a lesion, the addition of a guidewire provides haptic feedback when NPLs are being excised, increasing confidence in excision, saving time and minimizing the extent of resection.

Intraoperative ultrasound-guided wire localization (IUGWL) of NPLs was introduced into our unit after initial evaluation. Here we report on the outcomes of this technique in comparison with the gold standard PUGWL.

Aim

To evaluate the surgical and oncological outcomes and viability of the IUGWL technique.

Primary outcomes

Reoperation rates, resection size as assessed by specimen weights and surgical complications in IUGWL and PUGWL.

Secondary outcomes

To assess the accuracy and precision of localization and specimen excision in both groups using specimen x-rays. To evaluate the learning curve for the IUGWL technique as part of the surgical training program. To evaluate the effect on operating theatre time of the IUGWL technique. To assess the cost–effectiveness of the IUGWL technique.

Patients & methods

Subject identification & data collection

We used an opportunistic study design using a convenient sample of routinely collected data from patients being managed for breast cancer at our institution.

Data between October 2014 and December 2018 were collected from the electronic records system EPIC®. Anonymized data were recorded and analyzed. Proportions were analyzed using Fisher's exact test, and means using Student's t test with Prism software (GraphPad, CA, USA); p-values <0.05 were statistically significant.

Consecutive cases between October 2014 and December 2018 were included in the study if they fulfilled all the following inclusion and exclusion criteria.

Inclusion criteria

Patients with documented NPL.

Patients with core biopsy-confirmed invasive cancer or high grade ductal carcinoma *in situ* treated with BCS.

Patients with NPL and a sonographically visible lesion or marker clip that could be localized using ultrasound guidance.

Patients who underwent PUGWL or IUGWL for BCS.

Patients who had an intraoperative specimen radiograph taken.

Exclusion criteria

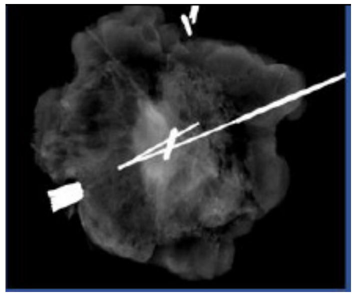
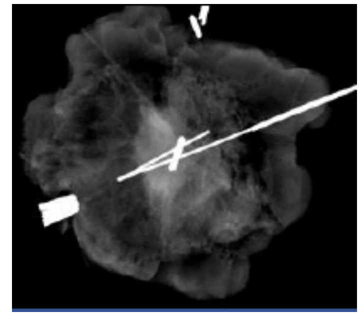
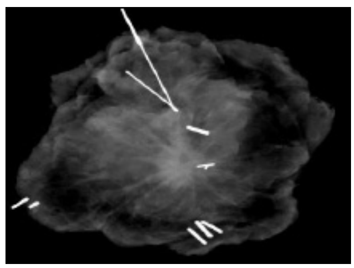
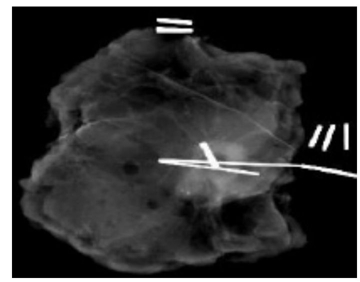
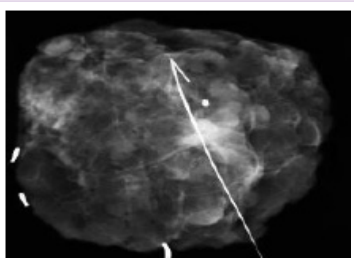
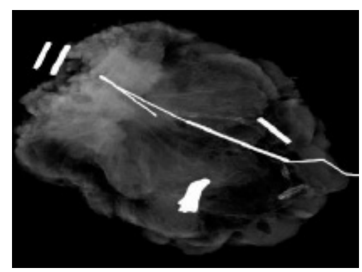
Patients undergoing diagnostic excision biopsies for benign or indeterminate lesions.

Patients undergoing therapeutic mammoplasties as BCS using either PUGWL or IUGWL.

Patients who underwent a combination of PUGWL and IUGWL for BCS.

Patients who underwent stereotactic guided wire localizations for NPL.

Table 1. Criteria for assessing the accuracy of localization and quality of the specimen excision.

Score	Localization accuracy		Lesion centricity in specimen	
1	Hook of wire within 20 mm of target		NPL or marker clip central and 5–20 mm from edges of excision	
2	Hook of wire within 20–30 mm of target		NPL or marker clip eccentric or more than 20 mm from one edge	
3	Hook of wire >30 mm from target		NPL or marker clip looks transected or <5 mm from one edge	

NPL: Nonpalpable lesion.

Primary outcomes

Primary outcomes were reoperation rates, specimen weights and surgical complications.

Reoperation rates were established using the number of patients in each group who either underwent re-excision or proceeded to mastectomy following BSC with positive margins.

Total specimen weight per resection was calculated, including any cavity shaves. Specimen weight is an accurate surrogate for volume [18]. If a patient had more than one lesion excised in separate specimens, each specimen was treated as a separate resection.

Surgical complications were any of the following: wound infection, hematoma, seroma, wound dehiscence, skin necrosis requiring further intervention or treatment. Follow-up was 10–48 months. The fully electronic patient records system EPIC® was used to identify complications.

Secondary outcomes

Accuracy & precision of localization & specimen excision

To assess the accuracy and precision of localization and specimen excision, two surgeons and one radiologist individually measured pre-agreed parameters, based on Quality Assurance Guidelines for Surgeons in Breast Cancer Screening [19] for anonymized specimen x-rays, and assigned a score as set out in Table 1. The closer to 1 the score, the more accurate the localization and the more centralized the lesion in the excision. Patients with more than one lesion had each lesion scored separately. A proportion of sequential patients were included in this part of the study, excluding those with no identifiable lesion or no guidewire on the specimen x-ray.

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Viability of IUGWL in training surgeons

To evaluate the learning curve for IUGWL, three senior breast trainees were given one-to-one training by a consultant surgeon. Once deemed competent, the trainees performed IUGWL independently. Training was evaluated with a questionnaire.

Evaluating the effect of IUGWL on operating theatre time

The electronic records system is updated in real time in the operating theatre. Events are recorded as: time into theatre, anesthetic start time, anesthetic ready time, knife to skin, operation finish time and time out of theatre. Assessment of surgical time was confined to patients undergoing excision of a single breast lesion either by PUGWL or with IUGWL. Anesthetic ready time to operation finish time was collected and analyzed.

Assessing the cost–effectiveness of IUGWL

The costing team in the hospital's finance department was asked to provide the breakdown and total cost of each procedure.

PUGWL method

PUGWLs are performed by a Radiologist on the day of surgery under local anesthetic in the Radiology department of the Breast Unit. The wire is dressed, and a two-view post-localization mammogram performed and reported. This entire process takes a minimum of 25 min per patient.

IUGWL method

IUGWLs are performed by the surgeon in the operating theatre. Once the patient is under general anesthesia, prepped and draped, the guidewire is inserted under ultrasound guidance. A post-wire mammogram is not required. No additional operating time is allotted for scheduling IUGWL cases.

A Sonosite Edge® (Amsterdam, Netherlands) ultrasound with a 15-6 MHz linear array probe is used to identify the target (either the lesion or a marker clip) in multiple planes. Our unit uses Hydromark® (Cincinnati, OH, USA) as a marker clip. We initially used a hook guidewire, but recently we have changed to an anchor guidewire which can be introduced one-handed: the Tuloc Premium, Somatex® (Berlin, Germany). An intraoperative specimen radiograph is taken to assess margins.

Results

511 patients were included in this study. 241 patients had PUGWL for 258 lesions, and 270 patients had IUGWL for 280 lesions.

Patient & tumor characteristics

All patients were female. The median age for PUGWL was 63 years (range: 29–86) and median age for IUGWL was 60 years (range: 21–86). 12% of patients in the PUGWL group were current smokers, compared with 9% in the IUGWL group. 69% of patients in the PUGWL group and 68% in the IUGWL group had recorded comorbidities. 97% of PUGWL patients and 96% of IUGWL patients were from a white European ethnic background. There was no significant different between PUGWL and IUGWL with regards to mean size of each index lesion (mm) targeted, patients with sonographic masses or type of disease (Table 2).

Primary outcomes

Primary outcomes for all cases included in this study are shown in Table 3.

Analysis of patients treated with primary surgery

Table 4 shows primary outcomes and tumour characteristics of patients treated with primary surgery.

Analysis of patients treated with neoadjuvant therapies

Table 5 shows the primary outcomes and tumour characteristics for patients who underwent neoadjuvant treatment.

Analysis of high grade ductal carcinoma *in situ*

Patients with high-grade ductal carcinoma *in situ* (DCIS) alone in the PUGWL group had an average lesion size on histology of 16 mm, versus 17.5 mm in the IUGWL group. The re-excision rate in the PUGWL group was 13/31

Table 2. Tumor characteristics for all patients included in this study.

	PUGWL	IUGWL	Total	p-value
Total number of patients	241	270	511	
Number of resections	248	273	521	
Number of lesions	258	280	538	
Patients with multifocal disease	16/241 (7%)	10/270 (4%)	26/511 (5%)	ns
Patients with sonographic mass	191/241 (79%)	213/270 (79%)	404/511 (79%)	ns
Patients who underwent neoadjuvant therapy	32/241 (13%)	62/270 (23%)	94/511 (18%)	ns
Invasive cancer +/− *in situ* component	217/248 (88%)	232/273 (85%)	449/521 (86%)	ns
Carcinoma *in situ* (high-grade DCIS)	31/248 (12%)	41/273 (15%)	71/521 (14%)	ns
Mean lesion size on histology (mm)	12.1 (0–47)	11.8 (0–50)		ns
Invasive cancer Grade 1, 2, 3, ungradable	61, 116, 39, 1	49, 114, 69, 0		0.01
Nodal status positive	26/217	33/232		ns

DCIS: Ductal carcinoma *in situ*; IUGWL: Intraoperative ultrasound-guided wire localization; ns: Not significant; PUGWL: Preoperative ultrasound-guided wire localization.

Table 3. Primary outcomes of all preoperative versus intraoperative ultrasound-guided wire localization patients.

	PUGWL	IUGWL	p-value
Mean specimen weight per resection (g)	34.2 (range: 3.7–155)	24.3 (range: 3.1–176)	<0.0001
Complication rate	14/241 (5.8%)	18/270 (6.6%)	0.72
Reoperation rate	44/248 (17.7%)	38/273 (13.9%)	0.28

There was a significant difference between the mean specimen weights per resection in each group: the IUGWL group had lower specimen weights. There was no significant difference in the reoperation rate or complication rate.
IUGWL: Intraoperative ultrasound-guided wire localization; PUGWL: Preoperative ultrasound-guided wire localization.

Table 4. Analysis of all patients in preoperative and intraoperative ultrasound-guided wire localization groups who had primary surgery.

	PUGWL	IUGWL	p-value
Total number of patients	209	208	
Median age (years)	65 (range: 29–86)	61 (range: 37–86)	ns
Number of lesions	224	216	
Number of resections	215	211	
Mean specimen weight per resection (g)	34.2 (range: 4.9–130)	22.8 (range: 3.1–105.3)	<0.0001
Complication rate	10/209 (4.9%)	12/208 (5.7%)	ns
Reoperation rate	41/215 (19%)	35/211 (16.5%)	ns
Mean lesion size on histology (mm)	13.1 (range: 1–47)	12.9 (range: 1.5–40)	ns
Invasive cancer grade 1, 2, 3	61, 101, 22	48, 96, 26	ns
Nodal status positive	23/184	21/170	ns
High grade DCIS	31/215	41/211	

There was a significant difference in the specimen weights between PUGWL and IUGWL patients. IUGWL patients had a smaller average specimen weight. There were no significant differences in any of the other outcomes.
DCIS: Ductal carcinoma *in situ*; IUGWL: Intraoperative ultrasound-guided wire localization; ns: Not significant; PUGWL: Preoperative ultrasound-guided wire localization.

(42%) and in the IUGWL group 7/41 (17.5%) (p = 0.03). The average weight of the resection in the PUGWL group was 32.9 g and in the IUGWL group was 20.5 g (p = 0.01).

Secondary outcomes

To assess quality measures, learning curve, cost effectiveness and effect on operating theatre time of IUGWL compared to PUGWL.

Quality measures of localization & excision

A total of 334 patients (171 PUGWL and 163 IUGWL) were included in this analysis (Table 6).

Table 5. Primary outcomes for patients who underwent neoadjuvant treatment.

	PUGWL	IUGWL	p-value
Total number of patients	32	62	
Number of lesions	34	64	
Number of resections	33	62	
Median age (years)	55 (range: 29–69)	54 (range: 21–77)	
Mean specimen weight per resection (g)	33.9 (range: 3.7–155)	29.4 (range: 4–176)	ns
Complication rate	4/32 (12.5%)	6/62 (9.7%)	ns
Reoperation rate	3/33 (9%)	3/62 (4.8%)	ns
Mean size per lesion on histology (mm)	5.5 (range: 0–27)	7.9 (range: 0–50)	ns
Invasive cancer grade 1, 2, 3, unable to grade	2, 13, 17, 1	1, 19, 42, 0	
Nodal status positive	3/33	12/62	

There was no significant difference in the average specimen weight, reoperation rate or complication rate between the two groups for patients who underwent neoadjuvant treatment.
IUGWL: Intraoperative ultrasound-guided wire localization; ns: Not significant; PUGWL: Preoperative ultrasound-guided wire localization.

Table 6. Accuracy of preoperative versus intraoperative ultrasound-guided wire localization.

Localization accuracy	PUGWL (n = 167)	IUGWL (n = 161)
1 = High level of accuracy	140 (84%)	137 (85%)
2 = Medium level of accuracy	18 (11%)	17 (11%)
3 = Low level of accuracy	9 (5%)	7 (4%)
Lesion centricity in specimen	**PUGWL (n = 171)**	**IUGWL (n = 163)**
1 = Lesion central	78 (45%)	89 (55%)
2 = Lesion slightly eccentric	61 (36%)	55 (34%)
3 = Lesion eccentric or transected	32 (19%)	19 (11%)

Values for accuracy and specimen excision quality should be as close to 1 as possible. The two groups have similar results in both categories.
IUGWL: Intraoperative ultrasound-guided wire localization; PUGWL: Preoperative ultrasound-guided wire localization.

IUGWL effect on operating time

To establish whether using IUGWL has any effect on operating times, 175 patients in each group having excision of a single lesion were identified. Data recorded in real time for anesthetic ready time and operation finish time were collected and analyzed. The PUGWL group had a mean operating time of 85 min, while the IUGWL group had a mean operating time of 78 min ($p = 0.002$).

Trainees evaluation of learning curve

The three senior surgical trainees reported that they were able to perform the IUGWL procedure independently after 15 proctored insertions, taking a maximum of 5 minutes per procedure. There were no misplaced wires or wire-related complications during the training phase or afterward. All three trainees reported that they will incorporate the technique into their consultant practice. They would also recommend the technique to other trainees and feel competent to teach the technique.

Cost–effectiveness of IUGWL

PUGWL costs £326 per procedure, including the cost of a post-localization mammogram.

IUGWL adds no operating theatre time. The additional disposables (guidewire plus sterile ultrasound probe cover) cost £37 per case. This represents a cost saving of £289 per case, or £80,920 for the 280 NPLs excised using IUGWL in this study.

The use of IUGWL also frees approximately 25 min of radiology time per case.

Discussion

Techniques for dealing with NPLs have been discussed since 1966 [20]. Over time, the National Health Service Breast Cancer Screening Programme and neoadjuvant therapies have established NPLs as a regular feature on operating theatre lists. Preoperative wire localizations became the gold standard for excision of NPLs, with many surgeons adapting to the technique and demonstrating good results [21–24]. The drawbacks are discomfort and stress for the patient [25], impact on list planning and breast clinic, pressure on radiology services and potential for wire migration. IUGWL obviates these issues.

Ultrasound was introduced into preoperative wire localizations in the early 1990s [26]. By the turn of the century intraoperative ultrasound was being explored by many. Initially a tool for simple identification of NPLs intraoperatively, its role was extended to assessing resections and cavities to ensure clear margins. Many studies on intraoperative ultrasound without the use of wires show good results with good rates of clear margins. They also testified to the ease of learning breast ultrasound [27–33].

The scope of intraoperative ultrasound has widened with the use of hydrogel marker clips which made NPLs not normally visible on ultrasound sonographically localizable, thus allowing pathology such as high grade DCIS to be managed with IUGWL.

The use of intraoperative ultrasound combined with surgeon-performed wire localization intraoperatively has only been mentioned in a few studies. Previous studies have reported that intraoperative ultrasound localization using a guidewire or marking needle is a safe technique for NPLs, with good outcomes [34–36]. Our study reports outcomes for the largest number of patients (511 compared with the 214, 28 and 32 from the previous similar studies). Two of the three previous studies focused only on NPLs, as does ours. Shin *et al.* reported a total of 214 patients, including only those with invasive cancer with or without associated DCIS [34]. Our cohort of patients includes those with only invasive cancer, only high-grade ductal carcinoma *in situ* and mixed disease. Our study shows favorable re-excision rates and specimen weights with the use of IUGWL for patients with high-grade DCIS alone when compared with PUGWL.

Ultrasound can be used to image the target before and after the wound is open without the use of a guidewire. Indeed, some NPLs can be palpable after initial dissection. Many NPLs, however, remain impalpable after initial dissection. This is particularly the case in NPLs marked with a marker clip, which can be lost during surgery. A skin marker alone, however, is not as helpful as using a guidewire [37].

The haptic feedback from the wire helps orientate the surgeon once the wound is open and tissue mobilized, especially in high-volume less dense breasts. The wire assists in centralizing the lesion in the specimen. Repeated ultrasound inside the wound can be time-consuming. The newer wires allow for a one-handed localization technique to deploy and anchor the wire, with a much-reduced risk of accidental dislodgement. The presence of a guidewire can increase confidence in excision, particularly in the event of loss of a marker clip. By placing the guidewire intraoperatively the surgeon is not limited or constrained in their incision or resection as they may be with PUGWL.

Our study used an opportunistic study design aimed at evaluating the safety and applicability of a technical innovation, by comparing it with a conventional technique. Such a design has inherent limitations, and the study is not intended to provide proof of noninferiority. However, the sample is one of the largest for this type of study reported in the literature, and the results for the IUGWL group are highly reassuring and should encourage others to evaluate the technique in other institutions and settings.

The patients in this study were allocated to either IUGWL or PUGWL according to which operating lists they were assigned to and who they saw in clinic. However, the patient groups had similar characteristics and disease profiles. While patients for primary surgery are assigned to the next available lists, neoadjuvant patients are referred to particular surgeons, and this may have resulted in a greater preponderance of patients operated on after neoadjuvant chemotherapy in the IUGWL group (accounting for the greater number of grade 3 cancers in this group). However, when the primary surgery and neoadjuvant groups were analyzed separately (Tables 4 & 5), the outcomes were similar for each subgroup. All operations in the IUGWL group were carried out by or supervised by one consultant; however, all were treated according to similar protocols, and all decisions regarding treatment were made by a multidisciplinary team.

Smaller excisions correlate with improved quality of life measures [38]. The IUGWL group had statistically significantly lower specimen weights without increased reoperation rates. Despite the time required for intraoperative guidewire insertion, the IUGWL operations took approximately 10% less time. We suggest that IUGWL affords the surgeon more confidence in their resection and the centricity of the lesion in the specimen and allows the surgeon to complete the resection more easily, as reflected in reduced operating time. The accuracy of localizations and excision, as assessed by specimen radiographs, were equally good between the two groups.

The viability of any new surgical technique depends on the transferability of skills. We assessed the training needs in IUGWL and found that trainees feel competent to perform the procedure independently after 15 supervised

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attempts. There is good concordance in the trainee feedback, and we plan to extend the trainee evaluation of this study.

The Royal College of Radiologists workforce consensus report in 2018 [39] explains the shortfall in radiologists across the UK, with many hospital trusts struggling to fill the gaps. The pressure on radiology departments throughout the UK continues to mount and is projected to get worse over the next 5 years. Solutions like IUGWL have been welcomed in our department, bringing benefits to both the multidisciplinary team and the patients. We estimate that our unit has saved £80,920 using this technique between October 2014 and December 2018.

During the COVID-19 pandemic, limiting patient and clinician exposure to what is deemed essential has been part of the strategy to prevent the spread of the virus. The use of the IUGWL technique has proven particularly useful for our unit and our patients during this period. Patients post-chemotherapy and others with NPLs have continued to have surgery during the pandemic.

Not only does the use of IUGWL decrease the footfall across the hospital and reduce exposure for patients and staff, but it has also allowed us to continue operating on patients with NPLs off the main hospital site without having to transfer radiological support. It allows flexibility with operating theatre planning, including evening and weekend elective lists, when departments such as radiology are running on an emergency-only schedule. The use of IUGWL for suitable cases has allowed patients in this highly anxious time to have one less trip to hospital, avoiding close interaction with additional personnel (radiologists, radiographers, support staff) and reducing potential exposure to COVID-19 during times of national lockdown. Given the guidance from the Association of Breast Surgeons for the COVID-19 pandemic, many patients were started on primary endocrine treatment and operated on months later, some with good response and palpable lesions becoming NPLs [40]. Again, the benefit of IUGWL gave us a 'safety blanket' to be able to use ultrasound and localize the lesion if required in the operating theatre on a site without breast radiologists.

Conclusion

Our study supports the assertion that IUGWL performed by a surgeon is a safe and effective technical innovation in dealing with nonpalpable breast lesions. The technique is cost-effective and the skills required are easily transferable. It merits further dissemination and evaluation.

Future perspective

Nonpalpable lesions are very common in our clinical practice and are expected to increase within the next 5–10 years considering the ever increasing technological advancements in imaging and screening techniques. New imaging modalities have been under investigation for risk stratification screening such as contrast enhanced mammography, automated whole breast ultrasound and abbreviated MRIs, which are proven to have higher diagnostic accuracy and cancer detection rate than the conventional full field digital mammography (FFDM). To establish the ideal technique for localization of NPLs, future studies should focus on a technique that would minimize patient exposure and appointments, prevents or minimize distress and anxiety to the patient. The ideal technique allows flexibility in scheduling, allows the surgeon to feel confident in identifying the position of the nonpalpable lesion, enables the surgeon to excise the lesion with clear margins and conserve as much breast tissue as possible, allows the surgeon the freedom to place their incision and resect the lesion whichever way they think would provide the best outcome. All whilst being cost-effective and easy to learn and implement. There is continuing innovation in localization techniques for nonpalpable breast lesions such as 3D printing, radioactive seeds, magnetic seeds, carbon marking, radiofrequency identified tags, radioguided occult lesion localization, IUGWL, intraoperative ultrasound localization and indocyanine green. The trend is to move away from preoperative localization and likely to be replaced by one of the newer techniques with time and research. This may however be limited by the cost–effectiveness, learning curve and ease of implementation of these various techniques in individual units. Individual units are likely to adopt varying techniques. Ultrasound is already an easily learnt and universally available imaging technique and the skills required to use it intraoperatively require minimal training to learn. As different techniques evolve, it is likely we would resort to a transferable technique which can be used in any breast unit regardless of where the initial biopsy took place. In future, surgical trainees would benefit from training in breast ultrasound and IUGWL techniques to aid their surgical practice as it is a cost-effective, efficient and accurate method of localization as demonstrated in our study.

Summary points

Background

- Nonpalpable breast cancers are common and require localization in order to surgically excise them.
- Various techniques for localization are available, the gold standard is preoperative ultrasound-guided wire localization (PUGWL).
- An alternative technique employed by our unit is intraoperative ultrasound-guided wire localization (IUGWL).
- IUGWL has many advantages for the patient, surgeon and the breast unit, including freedom in list scheduling, creative freedom for the surgical incision, confidence for the surgeon in their excision, prevents stress and discomfort for the patient whilst awake. IUGWL frees up resources such as radiology time and saves the patient having further mammograms.
- IUGWL has a learning curve and needs adequate training in intraoperative ultrasound and localization.

Aims

- This study aims to assess the viability of the IUGWL technique.
- Here we assess the primary outcomes; re-operation rate, specimen weights and complication rate, and the secondary outcomes; accuracy and precision of localization and specimen excision, viability of IUGWL in training surgeons, evaluate the effect of IUGWL on operating theatre time and assess the cost–effectiveness of IUGWL.

Patients & methods

- Patients who underwent either PUGWL or IUGWL from October 2014 to December 2018 were included.
- Patients included were those with a nonpalpable invasive breast cancer or high grade ductal carcinoma *in situ* (DCIS) with a visible marker clip or lesion on ultrasound who underwent breast conservation surgery.
- Patient's who were excluded were those who had a benign or indeterminate lesion at core biopsy, those who had a combination of PUGWL and IUGWL, those who required a stereotactic guidewire localization and those who had a therapeutic mammoplasty.
- Data was collected from the electronic records system and analyzed using Prism software.
- A cost analysis of each procedure was conducted.
- Three senior surgical trainees evaluated their experience with the procedure and their cases were assessed for complications of localizations.
- To assess the impact of IUGWL on theatre operating time, real time data of anaesthetic ready time and operation finish time for comparable single lesion IUGWL and PUGWL cases were collected and analyzed.

Results

- 511 patients were included in this study. A total of 241 patients had PUGWL for 258 lesions, and 270 patients had IUGWL for 280 lesions.
- Overall there was a significant difference between the mean specimen weights per resection in each group: the IUGWL group had lower specimen weights. There was no significant difference in the reoperation rate or complication rate.
- We analyzed patients who had primary surgery and neoadjuvant treatment separately.
- In those patients who had primary surgery there was a significant difference in the specimen weights between PUGWL and IUGWL patients. IUGWL patients had a smaller average specimen weight. There were no significant differences in any of the other outcomes.
- In those patients who had neoadjuvant treatment there was no significant difference in the average specimen weight, reoperation rate or complication rate between the two groups for patients.
- To assess the accuracy and precision of localization and specimen excision in the PUGWL and IUGWL groups, a total of 334 patients' specimen x-rays (171 PUGWL, 163 IUGWL) were scored using specific criteria by two surgeons and one radiologist.
- IUGWL and PUGWL groups have similar results in both categories used to assess quality of localization and of excision.
- Comparing operating times in patients undergoing PUGWL versus IUGWL we found PUGWL group had a mean operating time of 85 min, while the IUGWL group had a mean operating time of 78 min ($p = 0.002$).
- Trainees evaluation of learning curve revealed that three senior trainees felt competent performing IUGWL after 15 proctored cases. They reported their intention to employ IUGWL in their consultant practice and felt confident to train others.
- Assessing the costs for each procedure found that using IUGWL saves £289 per case, or £80,920 for the 280 NPLs excised using IUGWL in this study. The use of IUGWL also frees approximately 25 min of radiology time per case.

Discussion

- Localization techniques for NPLs have been discussed since 1966.
- PUGWL is the current gold standard for localization but it has its draw backs and risks of complications.
- The use of intraoperative ultrasound has increased, with many studies exploring this technique.
- The use of intraoperative ultrasound combined with surgeon-performed wire localization intraoperatively has only been mentioned in a few studies.
- Our study focuses on invasive cancer with or without an *in situ* component as well as high grade DCIS.

Conclusion

- Our study supports the use of IUGWL in NPL. IUGWL is safe, cost effective with comparable re-operation rates and complication rates to PUGWL.

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Author contributions

P Wignarajah: concept, design, acquisition of data, analysis, interpretation of data, write-up of work. V Papalouka: analysis, review of work. P Forouhi: concept, design, analysis, review of work.

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Ethical conduct of research

The authors are accountable for all aspects of the work. The authors have ensured the integrity and accuracy of their work. All procedures followed were in accordance with the ethical standards. Informed consent was obtained from all patients for being included in the study.

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